EUROPEAN CHEMICALS AGENCY

Helsinki, 10 November 2017

Addressee: [redacted]

Decision number: CCH-D-2114376213-53-01/F
Substance name: Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid
EC number: 609-946-4
CAS number: 41637-38-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 07/06/2016
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats with the registered substance;**

2. **In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) with the registered substance;**

3. **In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method: OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2, test method: OECD TG 487) with the registered substance;**

4. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered substance, provided that both studies requested under 2. and 3. have negative results;**

5. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD 421/422) in rats, oral route with the registered substance;**

6. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2., column 2; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**

7. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309) at a temperature of 12 °C with the registered substance.** The biodegradation of each constituent and relevant impurity present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed as further specified in Appendix 1, section 7.

This can be done simultaneously during the same study;

8. **Identification of degradation products (Annex IX, 9.2.3.) using an appropriate test method with the registered substance;**

9. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305, aqueous exposure/dietary exposure with the registered substance.** The bioaccumulation of each constituent and relevant impurity present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable shall be assessed as further specified in Appendix 1, section 9. This can be done simultaneously during the same study;

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **17 March 2021**. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

TOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Your registration dossier contains for the following toxicological endpoints adaptation arguments in form of a grouping and read-across approach according to Annex XI, 1.5. of the REACH Regulation.

- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)
- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- *In vitro* cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

ECHA has assessed first the scientific and regulatory validity of your Grouping and read-across approach for toxicological endpoints in general before the individual endpoints (sections 1, 2, 3, 4, 5 and 6).

Grouping and read-across approach for toxicological information

You have sought to adapt the information requirements for the toxicological endpoints mentioned above by applying a read-across approach in accordance with Annex XI, Section 1.5. According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural aspects the chemical structures have in common and the differences between the structures of the source and registered substances[2]. The differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures.

There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Thus physicochemical properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[3]- (1) (Bio)transformation to common compound(s) and (2) Different compounds have the same type of effect(s).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

You consider to achieve compliance with the REACH information requirements for the registered substance Ethoxylated bisphenol A dimethacrylate (CAS 41637-38-1) using data of structurally similar substances Ethoxylated bisphenol A diacrylate (64401-02-1) and of 2 moles ethoxylated bisphenol A dimethacrylate as supporting data (hereafter the 'source substances').

Description of the grouping and read-across approach proposed by the Registrant

You have provided a read-across justification as a separate attachment in the endpoint summary in the registration. In summary you provide the following arguments to support the read-across approach: "*All the substances with a core made of ethoxylated bisphenol A and with acrylate/ methacrylate function at each end could be suitable as source chemicals to fill by read-across the registration dossier of the target substance: ethoxylated bisphenol A dimethacrylate (CAS N. 41637-38-1). This read-across approach is based on the hypothesis that substances with a very close degree of ethoxylation and either acrylate or methacrylate functions at each end would show similar biodegradation patterns. It is also based on the hypothesis that substances with acrylate functions would be more toxic than substances with methacrylate functions. Therefore, the read-across approach would be applied to all the endpoints in ecotoxicology and toxicology*".

ECHA further notes you have provided a data matrix for the physical and chemical data, the environmental fate and ecotoxicological data and toxicological data for Ethoxylated bisphenol A dimethacrylate (target substance), the Ethoxylated bisphenol A diacrylate (source substance) and the 2 moles ethoxylated bisphenol A dimethacrylate (supporting substance). For the registered substance physical and chemical data, environmental fate and data on short-term toxicity to aquatic invertebrates is provided. No toxicological data is provided with the registered substance.

[3] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

In summary, ECHA understands that you propose that the read-across is possible due to structural similarity, similar physico-chemical, ecotoxicological and toxicological properties and similar biodegradation patterns and that the acrylate-substituted substances can be considered "*worst case*" compared to the methacrylate-substituted substances. ECHA considers this as the hypothesis under which you make predictions for the properties listed above.

ECHA analysis of the grouping and read-across approach in light of the requirements of Annex XI, 1.5.

Structural similarity, similar physico-chemical, ecotoxicological and toxicological properties

Your proposed adaptation argument is that the similarity in chemical structure and in some of the physico-chemical/ toxicological properties between the source and registered substance is a sufficient basis for predicting the properties of the registered substance for other endpoints. Structural similarity is a prerequisite for applying the grouping and read-across approach. However similarity in chemical structure and similarity of some of the physico-chemical/ toxicological properties does not always lead to predictable or similar human health properties in all the other endpoints. Therefore, your justification based on structural similarity, similar physico-chemical, ecotoxicological and toxicological properties has not established why the prediction is reliable for the human health/ environmental end-points for which the read across is claimed.

Similar Biodegradation patterns

One important aspect in establishing that substances have similar effects or follow a regular pattern is the comparison of the biodegradation of the parent-target and parent-source substances. The source and target substances may have differences in metabolites and therefore expectations of differences in effects.

ECHA notes that you have provided some information on biodegradation of the target and source substances but you have not provided information of potential metabolites and how these structurally different metabolites could influence the prediction. Neither is there information on the rate of the biodegradation.

ECHA acknowledges that there might be a similar biodegradation pattern for all three substances but this is not supported by any data. However, it is also possible that the structural differences in substitution and ethoxylation may result in numerous structurally different biodegradation products which may result in significantly different toxicological properties.

Thus you have not demonstrated similar biodegradation patterns for the source and registered substances, and for this reason, you have not established a reliable basis for predicting the properties of the registered substance.

Moreover, even if the biodegradation pathways would lead to identical final biodegradation products and acrylate or methacrylate, you have not shown that such biodegradation would be sufficiently rapid that there is no biological exposure to parent compound or non-identical biodegradation products (intermediates). Your hypothesis of 'similar biodegradation patterns' does not provide a basis for predicting the (eco)toxicological properties of the parent and non-identical biodegradation products (intermediates), since these would be structurally different for the source and target substances.

You have referred to a scientific article by McCarthy and Wity (1997) which investigates metabolism rates by carboxylesterase of specific acrylate and methacrylate esters (not including the substances used in the proposed read-across) in an assay. However, this paper does not provide data on the source or registered substances, and ECHA considers that your hypothesis is not thereby supported.

Furthermore, you referred to "Specialty Acrylates and Methacrylates Group, Multifunctional Acrylates Category. SIDS Test Plan and Data Review. Prepared for: American Chemistry Council, Specialty Acrylates and Methacrylates Panel. Prepared by: Toxicology/Regulatory Services, Inc. August 5, 2004". However, this is not present in the registration dossier.

Lack of evidence that acrylate-substituted substances can be considered "worst case" compared to the methacrylate-substituted substances

No toxicological data is provided with the registered substance, and hence you have not established that the source substances are "worst-case" compared to the registered substance. ECHA considers that you have not otherwise provided a reliable basis for predicting the properties of the registered substance (see above), and so it is not possible to compare the properties of the registered and source substances to draw conclusions about which is worst. You have referred to a scientific article by McCarthy and Wity (1997) which investigates metabolism rates by carboxylesterase of specific acrylate and methacrylate esters (not including the substances used in the proposed read-across) in an assay. However, this paper does not provide data on the source or registered substances, and ECHA considers that your hypothesis is not thereby supported. For these reasons, ECHA considers that your hypothesis that the source substance is "worst-case" is not supported, and cannot form a reliable basis for predicting the properties of the registered substance.

Conclusion on the read-across approach

Additionally, ECHA has taken into account all of your arguments together. ECHA firstly notes that you have not provided a reasoning as to why these arguments add to one another to provide sufficient basis for read-across. Secondly, the defects of each individual argument are not mitigated by the other arguments you have provided, and so ECHA considers that the arguments when taken all together do not provide a reliable basis for predicting the properties of the registered substance.

Therefore, ECHA considers that this grouping and read-across approach does not provide a reliable basis whereby the human health effects of the registered substance may be predicted from data for reference substance(s) within the group. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation.

ECHA notes that there are specific considerations for the individual endpoints which also result in a failure to meet the requirement of Annex XI, 1.5, and these are set out under the endpoint concerned.

As described above, further elements are needed to establish a reliable prediction for toxicological or ecotoxicological properties, based on recognition of the structural aspects the chemical structures have in common and the differences between the structures of the source and registered substances. This could be achieved (if it is possible) by a well-founded hypothesis of (bio)transformation to a common compound(s), or that the registered and source substance(s) have the same type of effect(s), together with sufficient supporting information to allow a prediction of human health properties.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a sub-chronic toxicity study (90 day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing the following adaptation statement: *"A read-across is proposed between Ethoxylated bisphenol A diacrylate and Ethoxylated bisphenol A dimethacrylate. An oral 90-day repeated toxicity study on rats (OECD 408) is proposed to ECHA on Ethoxylated bisphenol A diacrylate (read-across)"*, and by providing study records for:

(i) a 28 day study (oral route) according to OECD 407/EU method B.7 (2012), GLP with an analogue substance (CAS RN 64401-02-1, Ethoxylated bisphenol A diacrylate/ Poly(oxy-1,2-ethanediyl), α,α'-[1-methylethylidene)di-4,1-phenylene]bis[ω-[(1-oxo-2-propen-1-yl)oxy...); and

(ii) a combined repeated dose toxicity study (oral, rats) with the reproduction/developmental toxicity screening test according to OECD 422/ EPA OPPTS 870.3650 (2013), GLP with an analogue substance (CAR RN not indicated, 2 moles ethoxylated bisphenol A dimethacrylate).

However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI; Section 1.5., because as explained above in Appendix 1, Grouping and read-across approach for toxicological information section of this decision, your adaptation of the information requirement is rejected.

Additionally, in respect of your adaptation statement, you have not provided any data for a repeated dose 90-day oral toxicity study with an analogous substance in your dossier. The studies provided fail to meet the requirement of Annex XI, 1.5 that they should cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter. Specifically, the "repeated dose 28-day oral toxicity study" (test method: OECD TG 407) and "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422) have exposure duration of less than 90 days.

In conclusion, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 5.0, December 2016) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure (QSPR estimate provided = 1.17e-7 Pa). Furthermore uses with industrial / professional / consumer spray application are reported in the chemical safety report. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In your comments, you have expressed your intention to perform an OECD 422 study with the registered substance and compare the results with the results of the acrylate-substituted analogue substance in order to decide on the need for a sub-chronic toxicity study. ECHA notes that at this tonnage level a sub-chronic toxicity study is an information requirement unless Annex IX column 2 or Annex XI adaptations apply. ECHA reminds that currently there is not an adequate sub-chronic study available in the dossier. Therefore, any such adaptation will be assessed in the follow up phase.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for an *In vitro* gene mutation study in bacteria (OECD TG 471) with the analogue substances Ethoxylated bisphenol A diacrylate and 2 moles ethoxylated bisphenol A dimethacrylate.

However, as explained above in Appendix 1, Grouping and read-across approach for toxicological information section of this decision, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.
ECHA considers that the bacterial reverse mutation test (test method EU B.13/14. / OECD TG 471) is appropriate to address the standard information requirement of Annex VII, Section 8.4.1. of the REACH Regulation.

In your comments to the draft decision you express your agreement to perform the test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471).

3. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

An "In vitro cytogenicity study in mammalian cells or an in vitro micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for an in vitro cytogenicity / micronucleus study (OECD TG 487) with two analogue substances Ethoxylated bisphenol A diacrylate and 2 moles ethoxylated bisphenol A dimethacrylate. However, as explained above in Appendix 1, Grouping and read-across approach for toxicological information section of this decision, your adaptation of the information requirement is rejected.

Consequently, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the in vitro mammalian chromosome aberration test (test method OECD TG 473) and the in vitro mammalian cell micronucleus test (OECD TG 487) are both appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

In your comments to the draft decision you express your agreement to perform the test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: In vitro mammalian chromosome aberration test (test method: OECD TG 473) *OR* in vitro mammalian cell micronucleus study (test method: OECD TG 487).

4. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

An "In vitro gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for an in vitro gene mutation study in mammalian cells (HPRT) (OECD TG 476) with two analogue substances Ethoxylated bisphenol A diacrylate and 2 moles ethoxylated bisphenol A dimethacrylate.

However, as explained above in Appendix 1, Grouping and read-across approach for toxicological information section of this decision, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA considers that the in vitro mammalian cell gene mutation tests using the – Hprt and xprt genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

In your comments to the draft decision you express your agreement to perform the test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: In vitro mammalian cell gene mutation test (test method: OECD TG 476 or OECD TG 490) provided that both studies requested under 1. and 2. have negative results.

5. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from in vitro methods that the substance may be a developmental toxicant. No such evidence is presented in the dossier. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing study records for a screening for reproductive / developmental toxicity study (OECD TG 421) with the analogue substance Ethoxylated bisphenol A diacrylate (CAS RN 64401-02-1) and an one-generation reproductive toxicity study (OECD TG 422) with the analogue substance 2 moles ethoxylated bisphenol A dimethacrylate.

However, as explained above in Appendix 1, Grouping and read-across approach for toxicological information section of this decision, your adaptation of the information requirement is rejected.

Consequently, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. As there is an information gap, it is necessary to provide information for this endpoint.

According to the test methods OECD TG 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments to the draft decision you express your agreement to perform the test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Reproductive/developmental toxicity screening test (test method: OECD TG 421) *OR* Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

Notes for your consideration

For the selection of the appropriate test, please consult ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7a, Section R.7.5 and 7.6 (version 6.0, July 2017). You should also carefully consider the order of testing especially the requested screening (OECD TG 421/422) and the developmental toxicity studies (OECD TG 414) to ensure unnecessary animal testing is avoided, paying particular attention to ECHA's end point specific guidance document[4].

6. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2. While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.5. by providing an adaptation *"A read-across is proposed for this endpoint. A developmental study on rat (OECD 414) is proposed to ECHA on Ethoxylated bisphenol A diacrylate (read-across), and on 2 moles ethoxylated bisphenol A dimethacrylate (read-across)"*.

However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI; Section 1.5. because you have not provided any data for a pre-natal developmental toxicity study with an analogous substance in your dossier.

[4] ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance Version 5.0, December 2016, p 461-2 (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf).

Furthermore, as explained above in Appendix 1, Grouping and read-across approach for toxicological information section of this decision, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments, you have expressed your intention to perform an OECD 422 study with the registered substance and compare the results with the results of the acrylate-substituted analogue substance in order to decide on the need for a pre-natal developmental toxicity study with the registered substance. ECHA notes that at this tonnage level a pre-natal developmental toxicity study in a first species is an information requirement unless Annex IX column 2 or Annex XI adaptations apply. ECHA reminds that currently there is not an adequate pre-natal developmental toxicity study in a first species available in the dossier. Therefore, any such adaptation will be assessed in the follow up phase.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

ECOTOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

7. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of simulation testing of the registered substance on ultimate degradation in water in the dossier.

You have sought to adapt this information requirement according to Annex IX, Section 9.2., column 2. You provided the following justification for the adaptation:

"In two closed bottle tests conducted according to OECD 301D testing guideline, biodegradation (ThO2) of 24% and 43% after 28 days were found for the test item. These tests were extended and biodegradations of 54% and 66% were reached at Day 63 and 60, respectively. Based on these results, the chemical safety assessment did not indicate the need to investigate further the biodegradation potential.

Therefore, based on the experimental results which show the high potential for ultimate biodegradation of the test item and in accordance with column 2 of REACH Annex IX, no further tests are proposed".

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Column 2 of Annex IX, Sections 9.2.
According to Annex IX, Section 9.2.1.2, column 2 of the REACH Regulation, simulation testing on ultimate degradation in surface water does not need to be conducted if the substance is highly insoluble in water or is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance was not readily biodegradable in two OECD 301D tests where biodegradation (ThO2) of 24% and 43% was achieved after 28 days. Additionally, the registered substance cannot be considered to be highly insoluble as the water solubility is indicated to be 1.89 mg/L.

Furthermore, ECHA notes that you have not provided adequate justification in your chemical safety assessment (CSA) or in the technical dossier for why there is no need to investigate further the degradation of the substance and its degradation products. Based on the provided screening level information in the dossier the substance can be considered as potentially P or vP. There is also no information on the degradation products and their fate. In addition, information on bioaccumulation is missing and has been requested in this decision. ECHA therefore considers that at this stage, the information in the CSA is not complete due to the information gaps addressed in this decision. On this basis, the CSA cannot be used to justify that there is no need to investigate further the degradation of the substance and its degradation products. ECHA considers that the information is needed for the PBT/vPvB assessment and for the identification of the degradation products in relation to the PBT/vPvB assessment.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of the REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The Guidance on information requirements and chemical safety assessment R.7b (version 4.0, June 2017) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment". The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-8 (version 3.0 February 2016) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. Performing the test at the temperature of 12°C is within the applicable test conditions of the Test Guideline OECD TG 309. Therefore, the test should be performed at the temperature of 12°C.

In the OECD TG 309 Guideline two test options, the "pelagic test" and the "suspended sediment test", are described. ECHA considers that the pelagic test option should be followed as that is the recommended option for P assessment. The amount of suspended solids in the pelagic test should be representative of the level of suspended solids in EU surface water. The concentration of suspended solids in the surface water sample used should therefore be approximately 15 mg dw/L. Testing natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable. Furthermore, when reporting the non-extractable residues (NER) in your test results you should explain and scientifically justify the extraction procedure and solvent used obtaining a quantitative measure of NER.

Section R.11.4.1 of The Guidance on information requirements and chemical safety assessment R.11 on PBT/vPvB assessment (version 2.0, November 2014), indicates that "constituents, impurities and additives are relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w)". Individual concentrations < 0.1 % (w/w) normally need not be considered. Before conducting bioaccumulation testing it is necessary to conclude on the persistency information for all relevant constituents present in concentrations of ≥ 0.1% (w/w).

The registered UVCB substance consists of several constituents in variable concentrations, hence it is necessary to assess the persistency of all relevant constituents, as set out above. In order to fulfil this information requirement and to reduce the likelihood that additional simulation tests may be required during the forthcoming substance evaluation process, you are therefore required to carefully consider whether one or more constituent(s)/fraction(s) of the substance may be more relevant for testing instead of testing the registered UVCB substance as such. In order to select appropriate constituent(s)/fraction(s) for simulation testing you should consider those constituents/fractions which are most relevant for PBT assessment while avoiding constituents which are likely metabolites of other present constituents. You shall clearly explain the choice of constituent(s)/fraction(s) and justify it in the study documentation provided.

In your comments on the draft decision you indicate an intention to perform an inherent biodegradability study to demonstrate non-persistence of the substance. ECHA notes that it is not clear whether you intend to conduct the inherent test(s) on the whole substance or whether a certain fraction or fractions will be used. The screening pass level for non-persistence of 70% in OECD 302 inherent studies is intended for mono-constituent or pure substances. For UVCBs such as the registered substance, careful interpretation of results is required to demonstrate non-persistence via inherent testing. One cannot easily assess the persistence of complex substances that contain many constituents using biodegradation testing methods that measure parameters such as CO_2 evolution or DOC removal, since these tests measure the properties of the whole substance but do not provide information on the individual constituents. In conclusion, ECHA considers that it is difficult to use inherent testing on the whole UVCB substance in the context of PBT screening but does not exclude this as a possibility if done correctly.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309) at a temperature of 12 °C. You shall provide information on the degradation of all relevant constituents present in concentration of ≥ 0.1% (w/w). Alternatively, you shall provide a justification for why you consider certain constituents present in concentration of ≥ 0.1% (w/w) as not relevant for the PBT/vPvB assessment.

Notes for your consideration

Before conducting the requested test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 4.0, June 2017) and Chapter R.11, Section R.11.4.1.1 (version 2.0, November 2014) on PBT assessment.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the test detailed above are available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

8. Identification of degradation products (Annex IX, 9.2.3.)

The identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

The biodegradation section in the technical dossier does not contain any information in relation to the identification of degradation products, nor an adaptation in accordance with column 2 of Annex IX, Sections 9.2 or 9.2.3. or with the general rules of Annex XI for this standard information requirement. "

According to Annex IX, Section 9.2.3., column 2 of the REACH Regulation, identification of degradation products is not needed if the substance is readily biodegradable. ECHA notes that based on the information in the technical dossier, the registered substance is not readily biodegradable in two OECD 301D tests as also discussed in section 7 above.

Furthermore, ECHA notes that you have not provided any justification in your chemical safety assessment (CSA) or in the technical dossier for why there is no need to provide information on the degradation products. ECHA considers that this information is needed in relation to the PBT/vPvB assessment.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

Regarding appropriate and suitable test method, the methods will have to be substance-specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition, degradation half-life, log Kow and potential toxicity of the metabolite may be investigated. You may obtain this information from the simulation study also requested in this decision, or by some other measure. You will need to provide a scientifically valid justification for the chosen method.

In your comments on the draft decision you indicate an intention to perform an inherent biodegradability study to demonstrate non-persistence of the substance. ECHA notes that it is not clear whether you intend to conduct the inherent test(s) on the whole substance or whether a certain fraction or fractions will be used.

The screening pass level for non-persistence of 70% in OECD 302 inherent studies is intended for mono-constituent or pure substances. For UVCBs such as the registered substance, careful interpretation of results is required to demonstrate non-persistence via inherent testing. One cannot easily assess the persistence of complex substances that contain many constituents using biodegradation testing methods that measure parameters such as CO2 evolution or DOC removal, since these tests measure the properties of the whole substance but do not provide information on the individual constituents.

In conclusion, ECHA considers that it is difficult to use inherent testing on the whole UVCB substance in the context of PBT screening but does not exclude this as a possibility if done correctly.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Identification of the degradation products (Annex IX, Section 9.2.3.) by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration

Before providing the above information you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

9. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2.of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of bioaccumulation in aquatic species in the dossier that would meet the information requirement of Annex IX, Section 9.3.2.

Instead, you have sought to adapt this information requirement by providing the following justification *"According to the Integrated Testing Strategy (ITS) in the section R.11.4.1.2, Chapter R.11 of the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), "[...] the P criterion should be investigated in order to prevent unnecessary testing of animals. Further bioaccumulation testing is only necessary, if the P criterion has been confirmed to be fulfilled for the substance." As the P criterion is not fulfilled for the test substance, the bioaccumulation test is waived to avoid any unnecessary testing of animals*".

ECHA notes that this justification does not meet the specific rules for adaptation of Annex IX, Section 9.3.2., column 2 or any of the general rules for adaptation of Annex XI. The registered substance is reported to have log Kow in the range of 5.30 - 5.62 for 73.3% of the components so there is clear bioaccumulation potential. Additionally, due to the information gap in simulation testing as addressed under section 7 of this decision it is not possible at present to conclude on the PBT/vPvB properties of the substance. ECHA considers that the information on bioaccumulation is needed for the PBT/vPvB assessment.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 3.0, June 2017) bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2.

ECHA Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If you decided to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision. You shall also attempt to estimate the corresponding BCF value from the dietary test data by using the approaches given in Annex 8 of the OECD 305 TG. In any case you shall report all data derived from the dietary test as listed in the OECD 305 TG.
Section R.11.4.1 of The Guidance on information requirements and chemical safety assessment R.11 on PBT/vPvB assessment (version 2.0, November 2014), indicates that *"constituents, impurities and additives are relevant for the PBT/vPvB assessment when they are present in concentration of ≥ 0.1% (w/w)"*. Individual concentrations < 0.1 % (w/w) normally need not be considered.

The registered UVCB substance consists of several constituents in variable concentrations which means that it is necessary to assess the bioaccumulation of all relevant constituents, as set out above. In order to fulfill this information requirement and to reduce the likelihood that additional tests may be required during the forthcoming substance evaluation process, you are required to carefully consider whether one or more constituent(s)/fraction(s) of the substance may be more relevant for testing instead of testing the registered UVCB substance as such.

In order to select an appropriate constituent or fraction for bioaccumulation testing you should consider those constituents/fractions which are most relevant for PBT assessment. The choice of constituent(s)/fraction(s) shall be clearly explained and justified in the study documentation provided.

In your comments on the draft decision you indicate an intention to perform an inherent biodegradability study to demonstrate non-persistence of the substance. ECHA notes that it is not clear whether you intend to conduct the inherent test(s) on the whole substance or whether a certain fraction or fractions will be used.

The screening pass level for non-persistence of 70% in OECD 302 inherent studies is intended for mono-constituent or pure substances. For UVCBs such as the registered substance, careful interpretation of results is required to demonstrate non-persistence via inherent testing. One cannot easily assess the persistence of complex substances that contain many constituents using biodegradation testing methods that measure parameters such as CO2 evolution or DOC removal, since these tests measure the properties of the whole substance but do not provide information on the individual constituents.

In conclusion, ECHA considers that it is difficult to use inherent testing on the whole UVCB substance in the context of PBT screening but does not exclude this as a possibility if done correctly.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Bioaccumulation in fish: aqueous or dietary bioaccumulation fish test (test method: OECD TG 305). You shall provide information on the bioaccumulation of all relevant constituents present in concentration of ≥ 0.1% (w/w). Alternatively, you shall provide a justification for why you consider certain constituents present in concentration of ≥ 0.1% (w/w) as not relevant for the PBT/vPvB assessment.

Notes for your consideration

Before conducting the above test you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version version 3.0, June 2017), Chapter R.11.4. and Figure R.11-4 on the PBT assessment for further information on the integrated testing strategy for the bioaccumulation assessment of the registered substance. You should revise the PBT assessment when information on bioaccumulation is available.

Deadline in the decision

In your comments on the draft decision you have requested an extension to the deadline in the decision from 30 to 40 months. You argue that the registered substance is a UVCB that can be considered a *"difficult-to-test"* substance and that additional time is needed for the analytical work and carrying out the tests.

ECHA-S agrees that this UVCB substance is a difficult to test substance and there may be a need to investigate whether testing of certain fractions is appropriate for persistence and bioaccumulation testing. Consequently, additional time can be granted and the deadline is extended to 40 months.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 23 November 2016.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and amended the deadline. ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-56 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2019.

2. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

3. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

4. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.